
Promotion of the induction of cell pluripotency through metabolic remodeling by thyroid hormone triiodothyronine-activated PI3K/AKT signal pathway.

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Public Summary:

The existing methods to generate induced pluripotent stem cells (iPSCs) from adult mature cells, like skin fibroblasts, are very inefficient and extremely time-consuming. Prolonged cell selection often causes subtle genetic and epigenetic abnormalities in stem cells. To clear this road block, we screened a variety of human growth factors and hormones. Interestingly, we found that human thyroid hormone triiodothyronine (T3) was a potent factor that enhances the conversion of human skin cells into therapeutic stem cells. We demonstrate that the potentiation of stem cell induction is related to metabolic remodeling activity. We further identify the activation of the T3-activated PI3K/AKT signal pathway as an underlying mechanism. These studies demonstrate that T3 enhances metabolic remodeling of donor cells in potentiating iPSC induction.

Scientific Abstract:

Generation of induced pluripotent stem cells (iPSCs) from somatic cells by defined factors is a mechanism-unknown, yet extremely time-consuming process. Inefficient reprogramming leads to prolonged periods of in vitro iPSC selection, resulting in subtle genetic and epigenetic abnormalities. To facilitate pluripotent reprogramming, we have identified the thyroid hormone triiodothyronine (T3) as an endogenous factor that can enhance reprogramming of human dermal fibroblasts (HDF) and umbilical cord mesenchymal stem cells (UCMSC). This potentiation of iPSC induction is associated with metabolic remodeling activity, including upregulation of key glycolytic genes, an increase in cell proliferation, and the induction of mesenchymal-epithelial transition (MET). We further identify the activation of the PI3K/AKT signal pathway by T3 as an underlying mechanism for the enhanced conversion to cell pluripotency in this model. These studies demonstrate that T3 enhances metabolic remodeling of donor cells in potentiating cell reprogramming.

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